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Association between Methicillin-Resistant *Staphylococcus aureus* Colonization and Infection May Not Differ by Age Group

Adebola O. Ajao, PhD[1], **Anthony D. Harris, MD, MPH**[1], **J. Kristie Johnson, PhD**[2], **Mary-Claire Roghmann, MD, MS**[1,3], **Eli N. Perencevich, MD, MS**[4], **Marin L. Schweizer, PhD**[4], **Min Zhan, PhD**[1], **Wilbur H. Chen, MD, MS**[5], and **Jon P. Furuno, PhD**[6]

[1]Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, Maryland [2]Department of Pathology, University of Maryland School of Medicine, Baltimore, Maryland [3]Veterans Affairs Maryland Health Care System, Baltimore, Maryland [4]Department of Internal Medicine, University of Iowa Carver College of Medicine, Iowa City, Iowa [5]Department of Medicine, University of Mary-land School of Medicine, Baltimore, Maryland [6]Department of Pharmacy Practice, Oregon State University/Oregon Health and Science University College of Pharmacy, Portland, Oregon

Abstract

We assessed whether age modified the association between methicillin-resistant *Staphylococcus aureus* (MRSA) anterior nares colonization and subsequent infection. Among 7,405 patients (9,511 admissions), MRSA colonization was significantly associated with infection (adjusted odds ratio, 13.7 [95% confidence interval, 7.3–25.7]) but did not differ significantly by age group.

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are associated with longer hospital length of stay, higher healthcare costs, and higher mortality than infections due to susceptible strains.[1] MRSA colonization often precedes MRSA infection among hospitalized patients.[2,3] Increasing age is associated with decreased host resistance and increased exposure to healthcare settings, yet the association between MRSA colonization and infection in different age groups has not been well described.

We aimed to assess whether the risk of MRSA infection associated with MRSA nasal colonization on hospital admission increases linearly with increasing age. Given the ongoing active surveillance and isolation of patients colonized with MRSA in Veterans Affairs and other acute care hospitals, this knowledge may help us understand which patients have the highest risk of MRSA infection given MRSA colonization. In addition, it may help target the use of mupirocin decolonization, thereby reducing selective pressure and prolonging the effectiveness of this therapy.

Address correspondence to Jon P. Furuno, PhD, OSU/OHSU College of Pharmacy, Department of Pharmacy Practice, 3303 SW Bond Avenue, CH12C, Portland, OR 97239 (furuno@ohsu.edu).

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METHODS

Study design and patient population

This study was approved by the Institutional Review Board of the University of Maryland, Baltimore. This was a retrospective cohort study of adult patients admitted to non–intensive care unit (ICU) wards at the University of Maryland Medical Center (UMMC) between February 1, 2007, and June 30, 2009, who had no history of MRSA colonization or infection.[4] During the study period, UMMC was a 648-bed urban tertiary care hospital in Baltimore, Maryland. On February 1, 2007, UMMC began performing hospital-wide MRSA-targeted surveillance to identify patients colonized with MRSA within 48 hours of hospital admission on the basis of a previously published prediction rule for MRSA colonization.[5] Patients deemed to be at high risk for MRSA colonization received anterior nares surveillance cultures. MRSA infections were determined by a senior infection preventionist using National Healthcare Safety Network criteria.[6] Surveillance nasal swabs were processed for MRSA by means of the GeneOhm MRSA assay (Becton Dickinson) in accordance with the manufacturer's instructions.

Data collection

Methods for data collection have been described elsewhere.[4] Briefly, all data were abstracted from the UMMC central data repository, which contains patients' demographic, microbiology, and pharmacy data. Aggregate comorbidity was measured using the Charlson comorbidity index.[7] Time at risk was measured as time from hospital admission until MRSA infection or discharge.

Statistical analysis

All statistical analysis was performed using SAS software, version 9.3 (SAS Institute). Logistic regression was used to assess the association between patients with MRSA nasal colonization within 48 hours of admission and MRSA infection developed 48 hours after admission. To assess whether the risk of MRSA infection associated with MRSA colonization increases linearly with increasing age, we categorized age into 10-year age groups except the youngest group, which included patients 18–30 years old, and the oldest group, which included patients older than 70 years. Stratified analysis was performed to assess whether age modified the association between MRSA colonization and MRSA infection. Statistical significance was defined as P less than .05. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were calculated and reported for each age category. Since patients were allowed to enter the study multiple times, we adjusted for the correlated error structure of the data (on the basis of the robust variance estimator) in the multivariable analysis.

RESULTS

During the study period, there were 26,855 admissions of adult patients aged 18 years or more to UMMC non-ICU wards. Approximately 10% of admissions (n = 2,666) were known to have prior history of MRSA on the basis of the results of positive cultures on previous admissions (n = 2,481) or positive clinical cultures obtained prior to surveillance culture collection (n = 185) on the index admission and were excluded from the study population to avoid overestimating the risk of MRSA infection. Among the patients who were asked the screening questions, 7,405 (9,511 admissions) were identified as high risk and received anterior nares surveillance cultures. Of these patients, 6,142 (83%) had 1 admission, and 1,263 (17%) had repeat admissions. Mean age was 52 years (standard deviation, 16 years), and 53% of the patients were male. The median Charlson co-morbidity index score was 2.00 (interquartile range, 3).

Approximately 10% (964) of high-risk admissions were colonized with MRSA on hospital admission, and 41 (4%) had a subsequent MRSA infection 48 hours after admission. Median time at risk was 9 days for patients with MRSA infection and 6 days for patients without MRSA infection. The most common infections were skin and soft tissue (32%), pneumonia (24%), surgical site (15%), bloodstream (12%), bone (10%), and urinary tract (5%). Patients colonized with MRSA on hospital admission were significantly more likely to have MRSA infection after 48 hours of hospitalization, adjusting for age, time at risk, and Charlson comorbidity index (AOR, 13.7 [95% CI, 7.3–25.7]). Time at risk (AOR, 1.02 [95% CI, 1.01–1.04]) was significantly associated with MRSA infection. Charlson comorbidity index (AOR, 0.90 [95% CI, 0.78–1.05]) and age (AOR, 0.99 [95% CI, 0.98–1.01]) were not significantly associated with MRSA infection. Age was not a significant confounder of the association, and age group did not modify the association between MRSA colonization and MRSA infection, as evident in the overlap of the CIs (Figure 1).

DISCUSSION

Our results support previous studies that have demonstrated an association between MRSA colonization and infection.[2,3] The risk of MRSA infection associated with MRSA colonization did not increase linearly with increasing age.

There are important clinical and methodological implications of identifying factors that modify the association between MRSA colonization and MRSA infection. First, this knowledge may help identify and target patients with the highest risk of MRSA infection given MRSA colonization, thus helping to reduce mupirocin use and associated selective pressure. Second, epidemiologic studies that assess age as a risk factor for MRSA infection must consider whether MRSA infections vary by age in their study population when choosing an analysis strategy. Some studies have treated age as a continuous variable, thereby assuming increased risk of infection as age increases.[2,8] However, this assumption may not always be true.

Although surgery and the presence of invasive devices have been identified as risk factors for MRSA infection, information on these variables was not available for this study.[9] In addition, we did not have data on MRSA infections that occurred after discharge, and the incidence of these infection may differ by age group.

In conclusion, the susceptibility to infection once colonized remains highly independent of age. Further research is needed to better understand this association and provide guidance for mupirocin use and for epidemiologic studies of MRSA infection.

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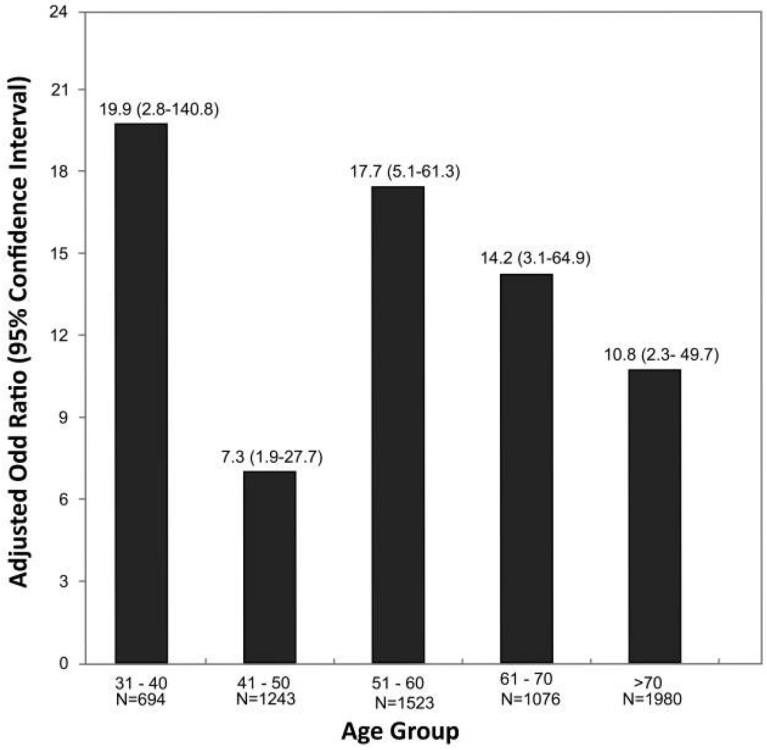

Figure 1.

Adjusted odds ratios and 95% confidence intervals for the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) infection associated with MRSA colonization by age group. Odds ratios were calculated using logistic regression and were adjusted for time at risk. The odds ratio for the age group 18–30 years was not computed because of small sample size and at least one 0 cell.